Oral Pathology(2)

Lec # 1 _ 14\2\2011

Chapter 11 : infections of the oral mucosa .

causative agents

As any infection in other parts of the body, causative agents of oral infections are:

- ♥ Viral agents,
- ♥ Bacterial agents,
- ♥ Fungal agents and,
- ♥ HIV & AIDS infections.

a- Viral infections

The most common viral infections of the oral cavity are the ***herpes simplex***.

herpes simplex is a member of family of viruses called ***herpes viridea*** , the members of this family are:

- ♥ *Herpes simplex I*, the most common causative agent of oral viral infections,
- ♥ *Herpes simplex II,*
- ♥ *Varicella – zoster,*
- ♥ *Epstien – Barr virus,*
- ♥ *Cytomegalovirus,*
- ♥ *Herpes simplex VI,VII,VIII*

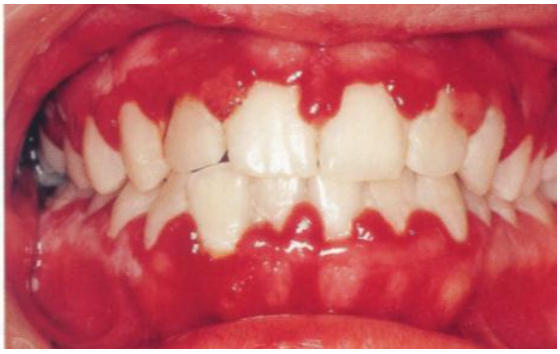
Herpes simplex I cause **primary herpes simplex infection** & **recurrent herpes simplex infection.** >>> Most of these viruses of this family can cause **primary infection** >> then they can stay **latent** >> then the might be triggered or stimulated to induce **secondary infection.**

The primary infection is sometimes **subclinical** (or asymptomatic) which is the interance of the virus to the body. Sometimes it may cause the **clinical features of a known disease**.

So again, the viral infection may be subclinical so that nobody can know it's there, or it might just have mild symptoms like: headache, fever, malaise, or it can cause the clinical features of a well-known disease.

After that latency will occur, for some viruses in the **nerve ganglion** and later on with a proper stimulant, reactivation will occur causing the secondary infection.

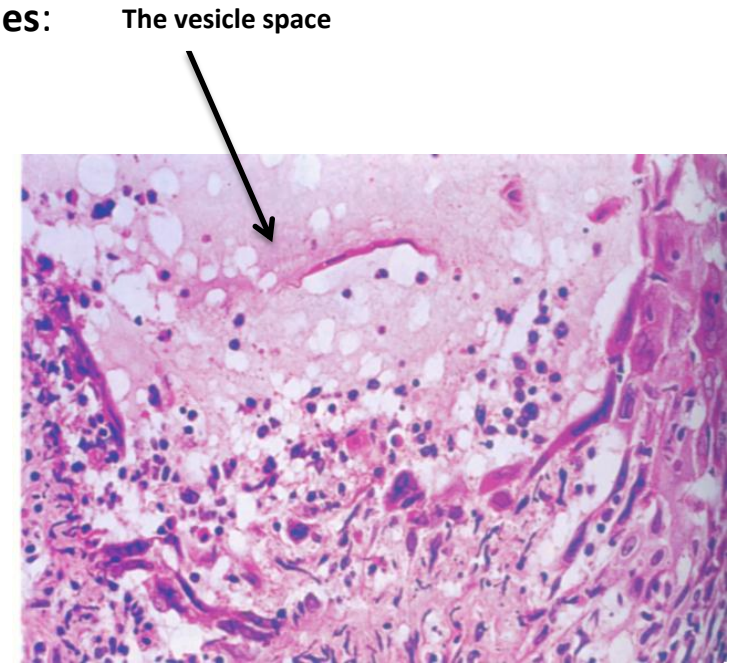
1- Herpes simplex I



It induces a **primary *Herpes simplex I viral* infection** in the oral cavity, this is known as **acute herpetic gingivostomatitis**.

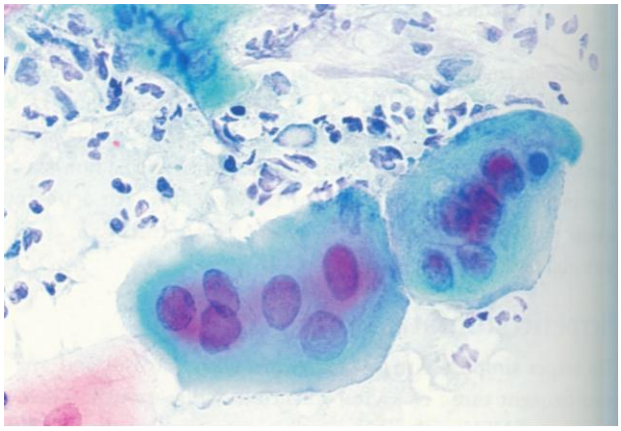
First of all, **an incubation period** of 5 days which is asymptomatic >> followed by **prodromal symptoms**: headache, fever, malaise, fatigue, etc...>> followed by small vesicles of 2mm in diameter, these will rupture quickly leaving ulceration.

Histopathology of the small vesicles:



the surface layer which is normally keratinized(not shown in this figure).

The space that you see is the vesicle which is **intraepithelial**>> it contain fluids, swollen detached epithelial cells with eosinophilic cytoplasm and with a large nucleus. The nucleus is filled with viral particles >> the virus is using the chromatin of the host cells to replicate >> when the cell enlarges to a certain size, it will rupture, spreading the virus to adjacent cells. These cells will be infected and will rupture later on leading to spread of more and more viruses…the dead cells will form this cavity and leakage of fluids from the surrounding tissue will make this small vesicle.



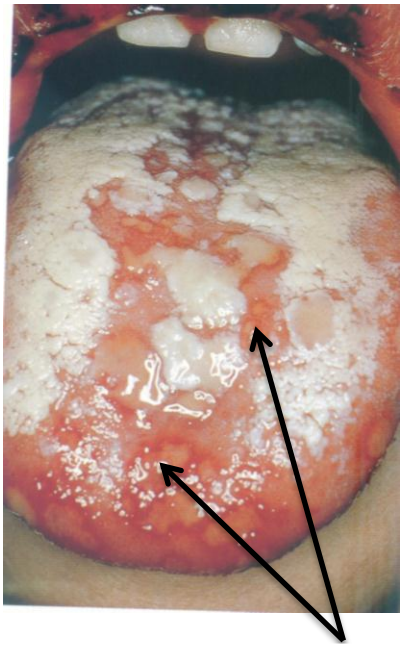
This virally infected cell with *Herpes simplex virus* is known as **Tzanck cell(**the T is sometimes silent**).** These cells show **ballooning degeneration**.

The **Tzanck cells** are *epithelial cells* which may be multinucleated >> sometimes the immune system starts secreting certain chemical mediators to induce formation of multinucleated giant cells for better defense. (Be careful!! These aren't macrophages or histiocytes that you see in granuloma, these are epithelial cells).

The *Herpes simplex virus* entered the body through the epithelial cells, started infecting the epithelial cells and caused the primary infection. Now, the recurrence usually (but not always) occur at the entrance site.

When the vesicles rupture, the virus will spread all over, and it will have access to the nerve endings of the sensory nerves which are everywhere in the body, then they will go up along the trigeminal nerve axon to the **trigeminal ganglion** in the brain.

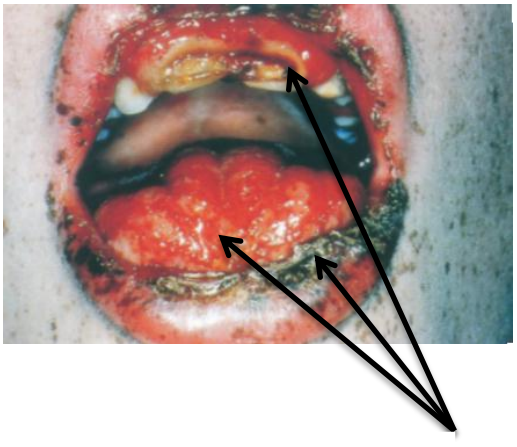
The primary infection is called **primary herpetic gingivostomatitis** (primary = for the 1st time, herpetic = herpes simplex, gingivo = involve the gingiva and stomatitis" an important feature" = involvement of the whole oral cavity" another important feature"). >> In the primary infection we see ulcerations on the gingiva and on the dorsal tongue (both have keratinized epithelium, keep this in mind because some other differential diagnoses will not occur on the gingiva, they will have ulcers but not on the gingiva or the tongue, we will talk about them later).



Dorsal tongue ulcerations

So, in **primary herpetic gingivostomatitis** we see :

- ♥ Tongue ulcerations,
- ♥ Gingival ulcerations,
- ♥ Ulcerations in other parts :lip or vermilion border with crusting, sometimes perioral crusting(oozing of exudate out of the vesicle leaving it dry causes crusting, this crusting can occur everywhere in the oral cavity as well as perioral).

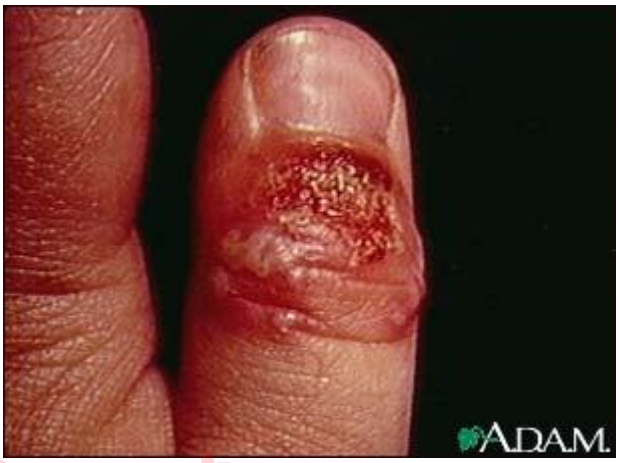


Crusting

How this will last?? And shall we give the patient antibiotic??

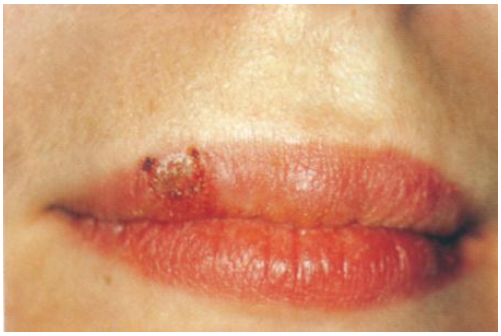
We don't give antibiotic as this is a viral infection unless we suspect a secondary bacterial infection. The virus is self-limited, it will heal in 14 days, this is very irritating and painful, the patient may take a pain killer and mouth rinses, he should also be encouraged to take high fluid amount and to consume soft food. It should be noted that the severity of the condition varies.

Herpetic whitlow is another common condition which is a charecterestic of dentists who work without wearing gloves , they will get it from a patient with primary or secondary herpetic infection, it's a primary infection by itself and its very painful.



Reactivation of the latent virus will cause a secondary infection. A common example is **recurrent herpes labialis,** it looks like a cold sore which appear after a common cold as a result of immune suppresion >> so,, the latent virus will be activated, moving along the nerve axon to the epithelium >> infection of the epithelium >> vesicles formation >> rupture of the vesicles >> crusting >> 10-14 days >> healing.

Recurrent herpes labialis may be bilateral, but its usually unilateral. The best location is the vermelion border and the junction of the vermelion border with the skin, it may occur on the filtrum or occasionally in the perioral area.



Factors that will lead to reactivation:

- ♥ Immunosuppresion,
- ♥ Sun exposure, use a good sun block with high SPF.,
- ♥ Stress , especially in exams time (just in JUST o_O)

Another form of secondary infections asocoiated with herpes semplex is **recurrent intraoral herpes infection**, it occurs on the hard palate, usually unilateral. The stimulating factor may be a truama from the preperation of a bridge, trauma from anesthesia, this is also a common problem after scaling of teeth >> the pateint comes to the oral diagnosis clinic complaining from vesicles not only on the hard palate but also on the gingiva surrounding the traumatized tooth >> tell the patient this is a reccurent viral infection and they will heal within 1-2 weeks without treatment. >> these vesicles are pin- pointed and usually asymptomatic or with very mild symptoms. >> follow up the patient to insure that healing occurred.

Recurrent and primary herpes infections have the same histopathologic features(vesicels and Tzanck cell formation).

2- Varicella- Zoster virus

It causes a primary infection which is the **chickenpox,** then it will go along the nerve and reactivation will cause the secondary infection which is **herpes zoster** or **shingles**.

The primary infection starts with prodromal symptoms: headache, fever, malaise, fatigue, lymphadenopathy, etc… >> then the vesicles start erupting in the abdomen and the trunk then to other parts of the body, these vesicles may be filled with fluids, ruptured, edematous, you can see them at variant stages of eruption and they are very itchy.

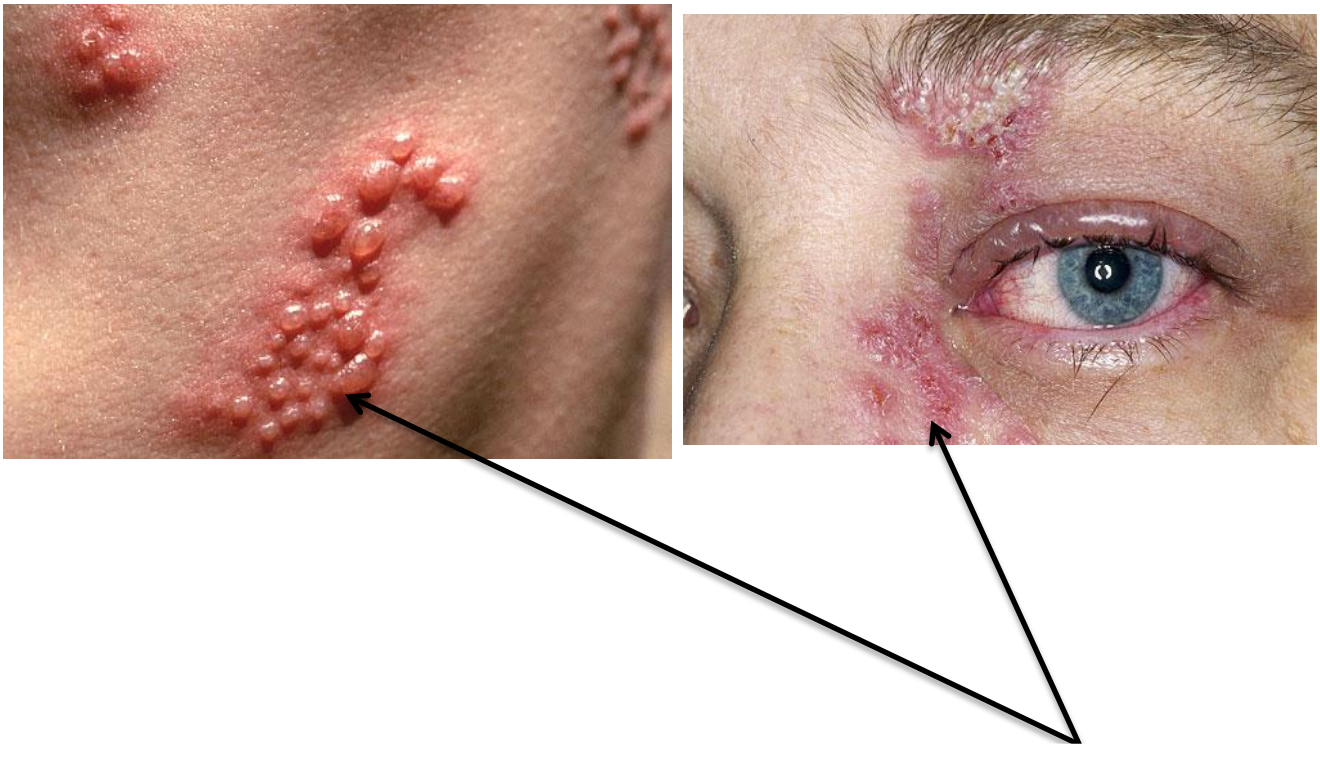
Intraorally, it appears in the soft palate and it's not really painful. The question is: how to distinguish it from primary herpetic gingivostomatitis?? Simply it's not only on the soft palate, its perioral and if you check the abdomen, you will find vesicles. In acute herpetic gingivostomatitis I should see gingival and tongue involvement plus they are painful.

Microscopically, they are identical to acute herpetic gingivostomatitis: vesicles, ballooning degeneration, Tzanck cells…

Vaccines are now available. Doctors think that they are good because they prevent shingles formation, which is very painful severe distressing disease with many complications. Treatment is antihistamines with topical lotions.

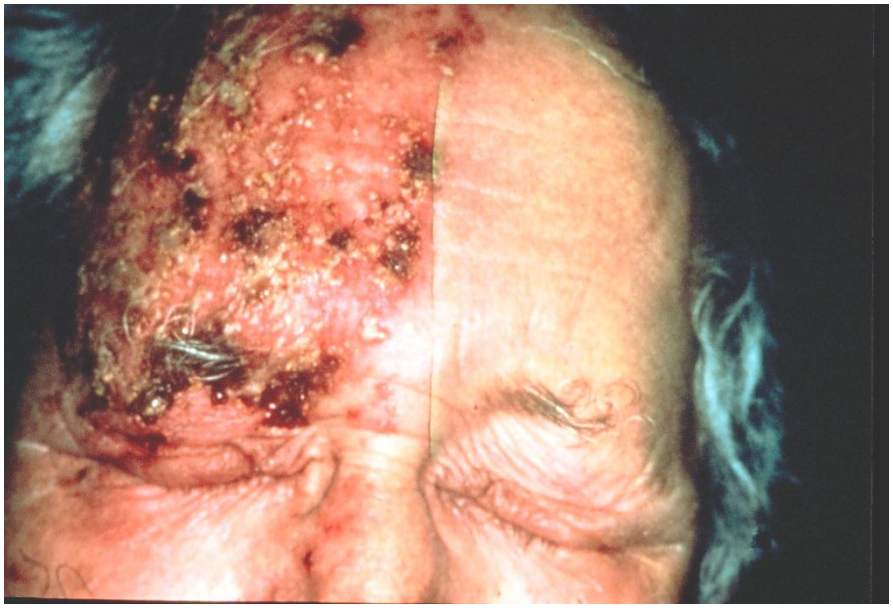
Multiple recurrence of herpes zoster is rare compared to herpes simplex; those with recurrent herpes labialis know that they have it once every month or every 3 months…but with shingles its rare (el7mdellah).

Latency occur in the trigeminal sensory ganglion in the oral cavity and face while in the dorsal root ganglion in the back.



Shingles

The predisposing factors are stronger than those that cause recurrent herpes : the patient is elderly >> decreased immunocompetence (may be due to certain medications e.g., corticosteroids, cyclosporine) >> so in shingles there is sever eruptions, ulcerations, crusting and **the most commonly involved branch of the trigeminal nerve is the ophthalmic** with complications affecting the eye >> sometimes you can demarcate a sharp line for the extension of the ulcers and the vesicles >> in a primary infection we see crossing of the midline and the lesion is always bilateral but in shingles its always unilateral >> its sever, involving wide areas, it may be intraoral and extraoral.



Complications include:

- **post-herpetic neuralgia** i.e., a pain that doesn't have a real treatment, this is chronic, distressing and the patient may need antidepressant just to live in an acceptable way.
- There may be **Ramsay –Hunt syndrome**, in which there is involvement of the geniculate ganglion(motor ganglion of the facial nerve), there may be facial nerve paralysis >> so, the patient may have facial palsy.
- Complications of the eye are also seen due to eye infection.

3- Coxsackievirus

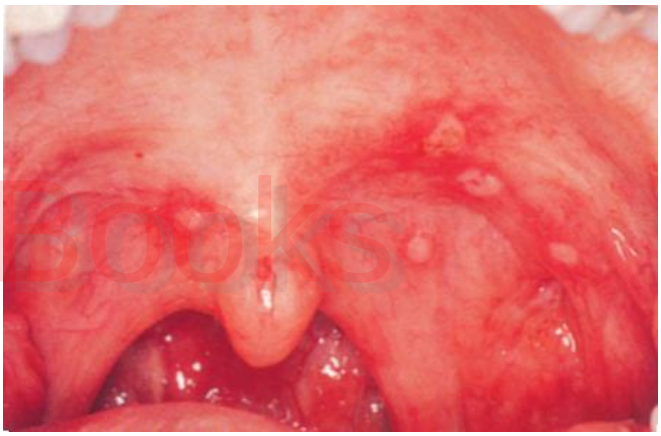
It’s a virus of the ***entero viridea*** family . it's an RNA virus

What are the diseases caused by this virus intraoraly ??

- ♥ Herpangina,
- ♥ Hand, Foot, and Mouth disease,
- ♥ Acute lymphonodular pharyngitis.

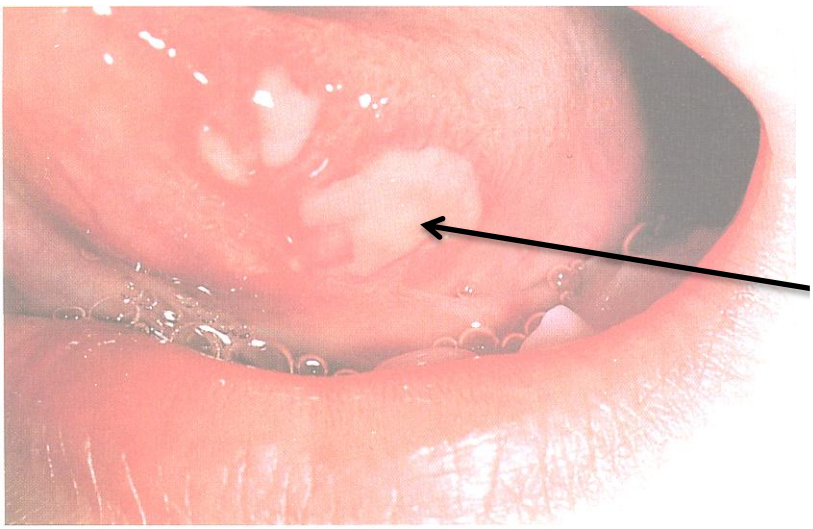
Herpangina

It's an endemic disease, occur mostly in childhood especially in nursery classes and kindergarten where almost all the class members are infected. its mild causing ulcerations and vesicles on the soft palate posteriorly (it likes to involve the post part of the oral cavity, unlike the herpes infection which involve the hard palate) >> we don’t see lesions on the tongue or the gingiva . it's not really symptomatic >>> so, when you see ulcers on the post part of the soft palate, don’t give the patient antibiotic because this is Coxsackievirus group A and it will just go away i.e., its self-limiting and has a sudden onset.

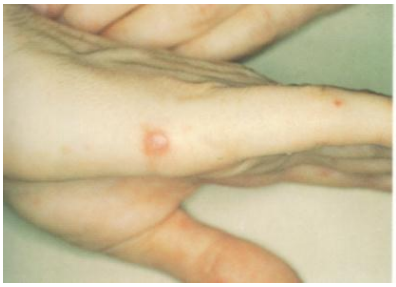


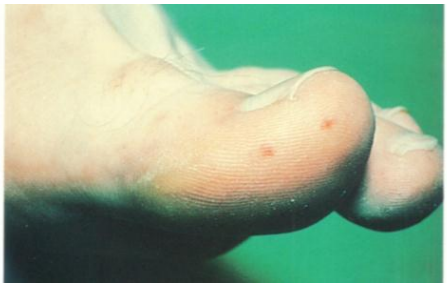
Hand, Foot, and Mouth disease

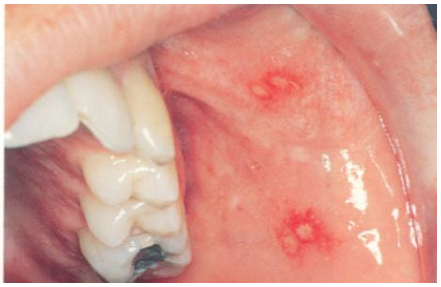
Caused by *Coxsackievirus A16* . It involves three areas : hand, foot and mouth, but the most constant feature is the mouth ulcerations, and these ulcerations like to involve the anterior part, being larger than the Herpangina >> clinically, the patient comes to your clinic complaining of these ulcerations with crusting which are large but don't involve the tongue or the gingiva >> you ask the patient : are these recurrent ulcers, he says: no >> look at the hands and the feet >> if you recognize other ulcerations on the palms and the souls >> this is hand, foot, and mouth disease >> this is self-limiting and won't stay for more than 10 days



This is a big ulcer involving the lateral border of the tongue



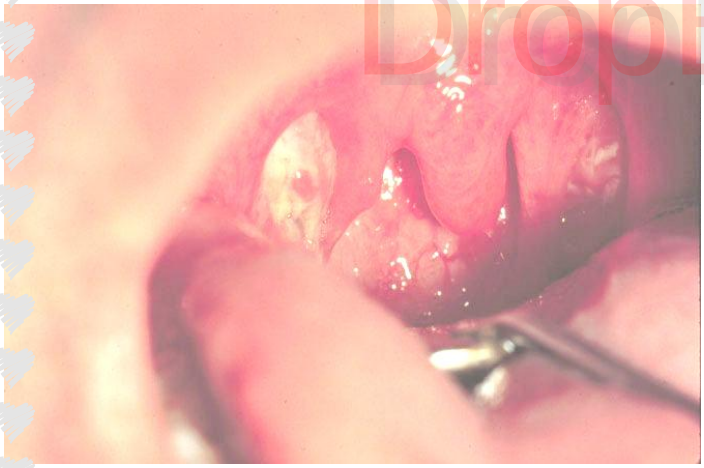


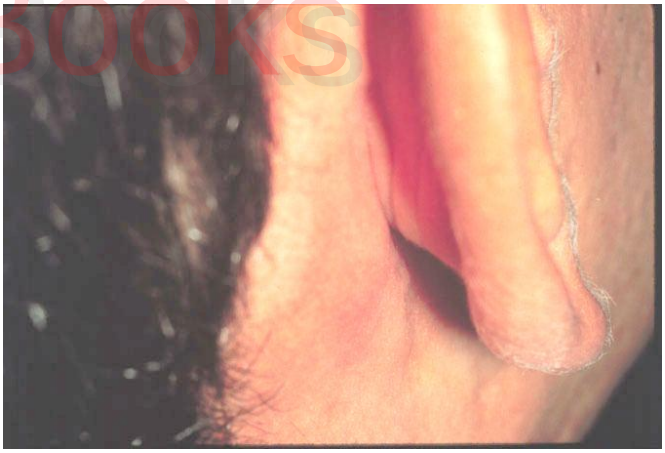


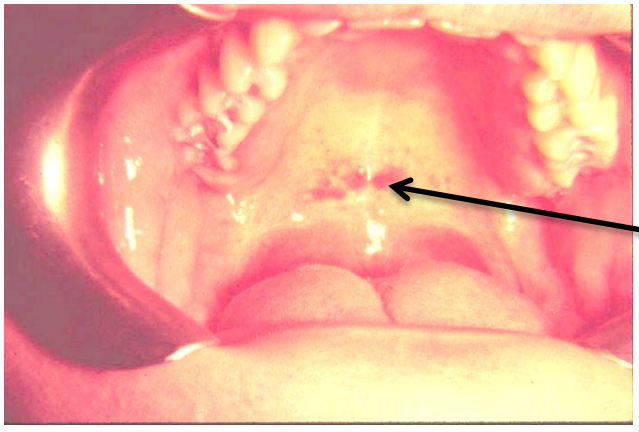
Infectious mononucleosis (Glandular fever)

Its caused by *Epstein-Barr Virus (EBV)* as a primary infection. The recurrent infection is **Hairy leukoplakia**. Latency of the virus will be in the **B-cells and the epithelial cells** >> for this reason the EBV is involved generally in the B-cell lymphomas >> latency of the virus for a long time isn't good because it will have the chance to induce DNA changes. **It is transmitted by saliva** >> all the lymph nodes in the neck will be involved: large,, tender and really painful with tonsillitis >> when the patient receive antibiotics, he will not heal >> some of the antibiotics will even induce skin rashes >> soo,, fever and prolonged malaise >> the problem is that after healing of the pharyngitis and the tonsillitis, the patient still feel tired and fatigued for weeks.

Cytollogicaly, we see abnormal, large peripheral lymphocytes.







Petechei, on the palate, they could caused by cough, but its associated with infectious mononucleosis

Measles:

caused by *Paramyxovirus*, affect children. Its reduced nowadays because of vaccination. Intraoral symptoms include **Koplik`s spots** i.e., white spots occur on the buccal mucosa and they disappear when the skin rash starts to appear >> rarely detected because when the patient is diagnosed with measles, they have already disappeared >> complications include

- ♥ brain damage in severe cases,
- ♥ encephalitis,
- ♥ otitis media, and
- ♥ pneumonia: due to spread of the virus
- ♥ Noma : gangerin of the perioral tissues in malnourished children or in immunocompromized patients.

4- Cytomegalovirus:

It`s in the family of ***herpes viridea*** >> it's a DNA virus >> it causes a primary infection in the neonates at the time of delivery >> it may stay latent in the endothelial cells (lining the blood vessels) or in the ductal epithelium >> it may be subclinical (in 40-60 % of the population), or clinical >> affects immunocompromized patients : neonates who still didn't develop a good immune system, transplant patients.

Recurrence occur intraoraly as atypical, non-specific oral ulcerations.

b- bacterial infections

1-Necrotizing ulcerative gingivitis (NUG)

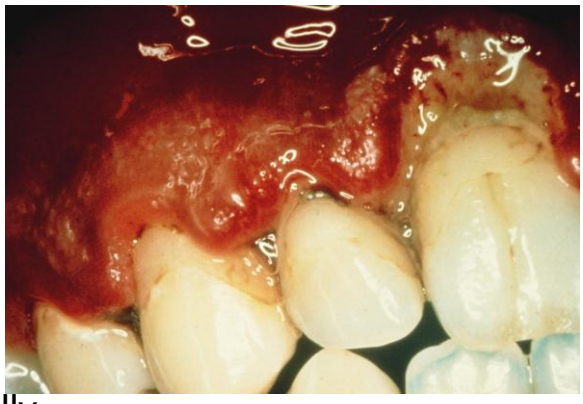
(Acute ulcerative gingivitis, acute necrotizing ulcerative gingivitis (AUG, ANUG)):

It is a type of Gingivitis But different than Common Gingivitis. (Marginal Gingivitis that most of the people have)

Gingiva is: free on peripheries and attached, which is attached to Bone (on space between it and the Bone) but the free Gingiva there is a pocket between the Gingiva and the teeth.

In ANUG loss of Interdental Papilla (part of free Gingiva between teeth) through Necrosis & some also from free Gingiva.

ANUG



Clinically
Ulceration of interdental papilla and gingival margins
Grey-green psuedomembrane
Halitosis, salivation, lymphadenopathy

In industrialized countries:

Mostly in young adults. More common in males than females

In developing countries:

In children due to poverty and malnutrition.

What is the Predisposing factor? This is a serious condition, it is the stressing Painful, and it will need medication for healing.

The difference in this kind of Gingivitis is that the Pt is immunosuppressed not due to medication or malignancies Transplant Pts , it is may be due to severe stress like soldiers in wars & smoking is another predisposing factor & malnutrition (mostly in soldiers) in addition to poverty & fatigue.

If u treated this Pt by curettage (Removal of Pseudomembrane) or by irrigation with medication Antibiotics by giving Pt Metronidazole even if u treated your Pt in a good way, this disease may be recur if u didn't remove the underlying factor by good eating, Stop smoking to improve Pt immunity.

Causative Agent: *Fusospinchaetal complex* which present already in our mouth.

But we need these underlying factors to Get the infection with these Bacteria so this is endogenous, what is the meaning of endogenous? It means that we have causative in our bodies but we it needs a good environment a good host situation to start casing the disease like the Fusospinchaetal complex which needs these factors to cause the ANUG.

Infection presents with necrosis and create-like, punched out ulceration of inter papillae of sudden onset which may involve gingival margins

There will be necrosis and Ulcers covered with grayish-green pseudomembrane demarcated from surrounding mucosa by linear erythema.

The Target is marginal Gingiva & Interdental Papilla. It may extend a little bit to the attached Gingiva but it is usually in Interdental Papilla & Marginal Gingiva.

Signs & symptoms:

Gingival bleeding, pain, soreness of gums, marked halitosis, bad taste (metallic) & increased salivation.

Pseudomembrane consists of necrotic tissue debris, inflammatory exudate and bacteria.

Bacteria types: *F. fusiformis & T. vincentii*

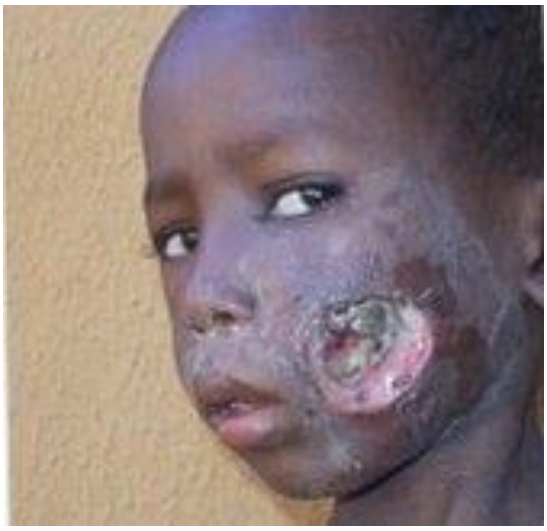
There are recurrence Rate if the underlying cause is not treated.

2- Noma (cancrum oris):

It is severe rapidly developing gangrene of orofacial tissues and jaws mostly occur in developing countries.

Majority of cases preceded by ANUG followed by rapid spread of necrosis from original gingival lesions into cheek and development of an area of demarcated gangrene of orofacial tissues if ANUG malnutrition stay & street & Pt is child living in poverty & doesn't have Good New system.

Same histological features of ANUG but *Fusobacterium necrophorum* and *prevotella intermedia* are key organisms.



3- Actinomycosis:

It is not fungal even if it is mycosis. It is Bacterial Infection , At is found normally but it needs entrance to induce this infection as it enters it reach to Bone or though the pulp.

It is a chronic, suppurative, polymicrobial infection caused by endogenous bacteria (*Actinomyces* species specially *Actinomyces israelii*), it is anaerobic bacteria.

In Actinomycosis other anaerobic bacteria are synergistic, help in the growth of Actinomyces.

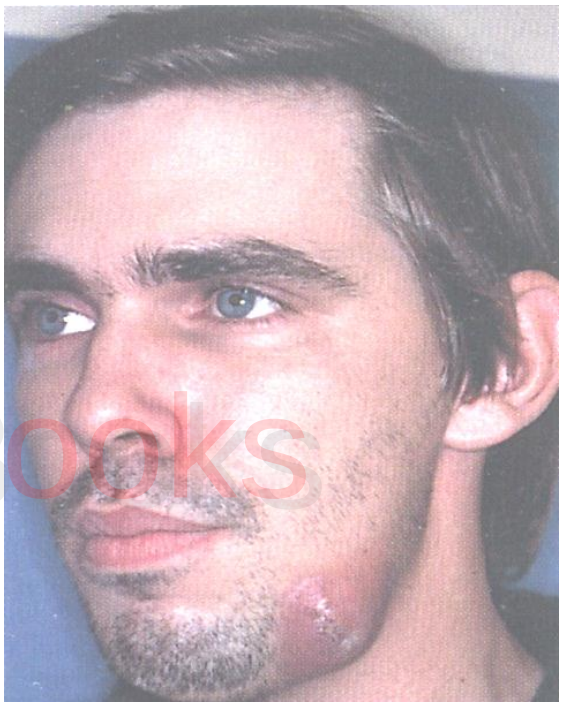
In **cervicofacial Actinomycosis**, soft tissue of submandibular area and neck involved.

Infection has multiple foci of chronic suppuration. It presents with development of firm swellings eventually soften and accompanied by formation of pus.

Abscess inside Bone >> pus formation >> Inflammation >> Then it will point out on the skin surface through sinus tracts sinus opening that Bus go out through it , drain out through sinuses opened on skin (face). Not inside the oral Cavity.

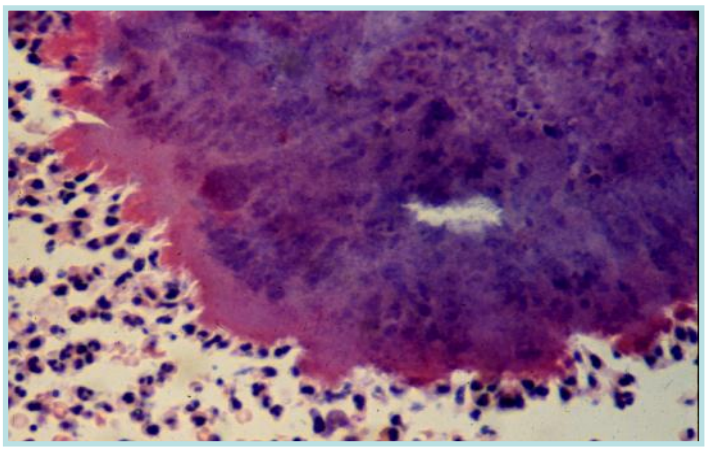
Painless even the swelling is painless.

Infection is **endogenous** and either tooth socket or infected root canal is the portals of entry.



When squeezing happened to this sulfur yellowish Granules will be released These Granules are Bacterial colonies as you see here. This is a big Bacterial colony which is calcified so it appears as a yellowish granules within the Bus which is present there. These are Bacterial colonies which have rods it Give u a sun Ray appearance and look at the peripheries all of these are neutrophiles, they are trying engulfing or attacking the Bacteria which is found.

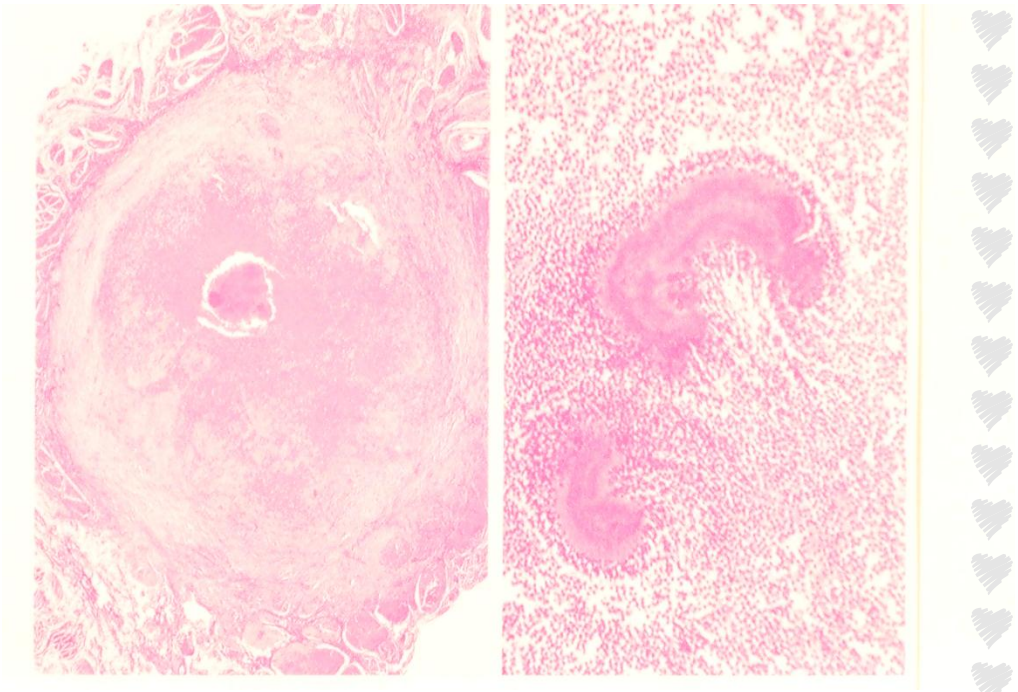
Microscopically, you will see Red & blue colon with neutrophiles & inflammatory cells trying to be attached to it & these colonies are big in size actually.



So you can see them easily on microscope.

At periapical lesion which we think it is a radiaular cyst but we can see some of these the Pt with antibiotics that the Pt has **Actinomycosis colonies** are different than Any other Bacteria, the treatment is 4 weeks with penicillin's.

First, it is firm swelling later on it will suppurate giving Bus that will point out on the skin.



Endogenous – Anaerobic so it lives inside the bone & it is Gum + ve.

4- Syphilis (primary, secondary, tertiary, and congenital):

It is an infection caused by *spirochaete Treponema Pallidum*.

♥ Primary lesion (chancre):

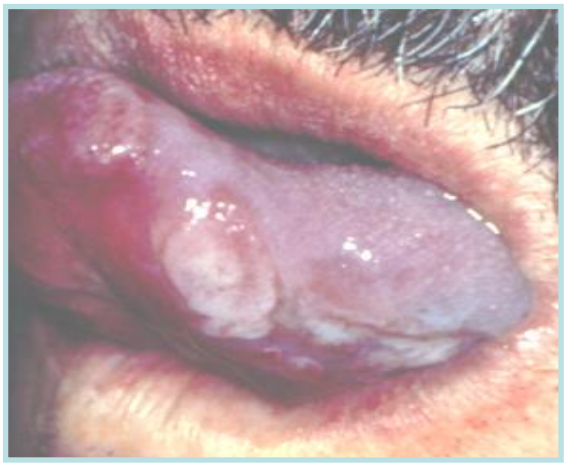
occurs on genitalia, minority of patients present on oral mucosa usually lips.

Ulcer: Shallow, non painful indurated Base as there is Granulomatous inflammation & there is a lot Bacteria here in this ulcer

Regional lymph nodes are enlarged.

Histologically: consist of ulcerated granulation tissue with dense mononuclear inflammatory cells (plasma cells).

Mononuclear means not neutrophils. (Not neutrophilic infiltrate mainly plasma cells

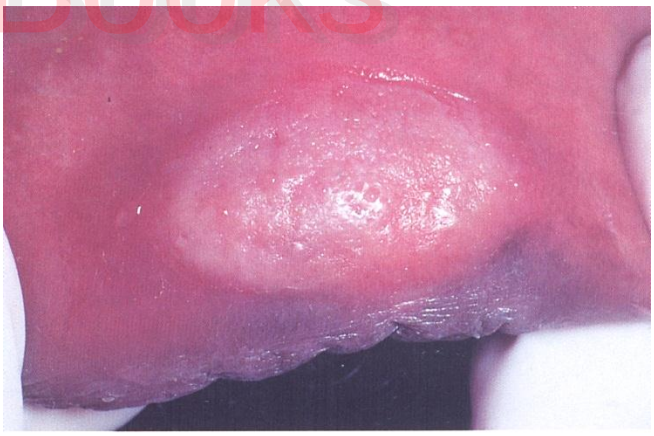


Healing spontaneously within 3-6 weeks (not a short duration)

The Pt in week #5 may wrong about other causes cytomegalovirus or malignancies or fungal infections.

- **Secondary syphilis**

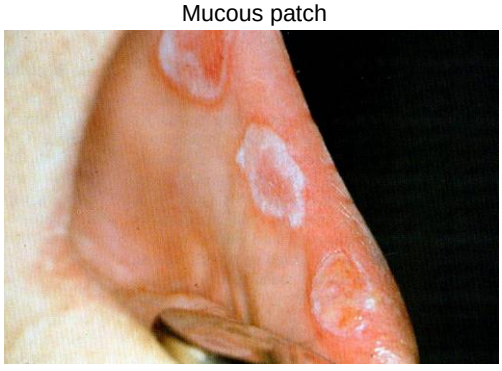
It develops about 6 weeks after appearance of primary chancre, some 2-3 months after initial exposure.



There is a generalized skin rash may be accompanied by oral lesions of which the mucous patch is most frequent.

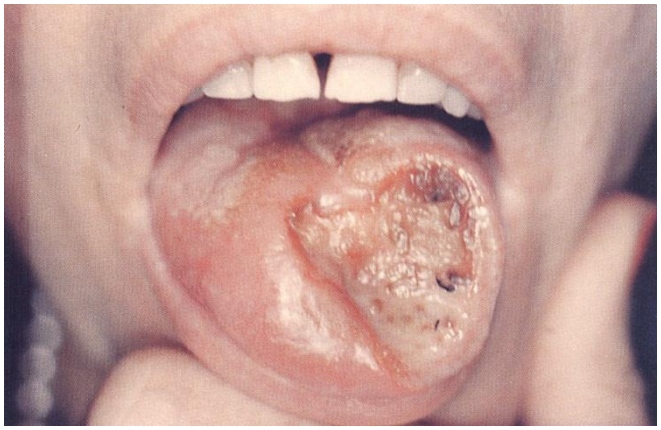
Mucous patches are flat areas of ulceration, mostly multiple and may coalesce to produce lesions of irregular outline called Snail-Track Ulcer.

Syphilis
Mucous patch

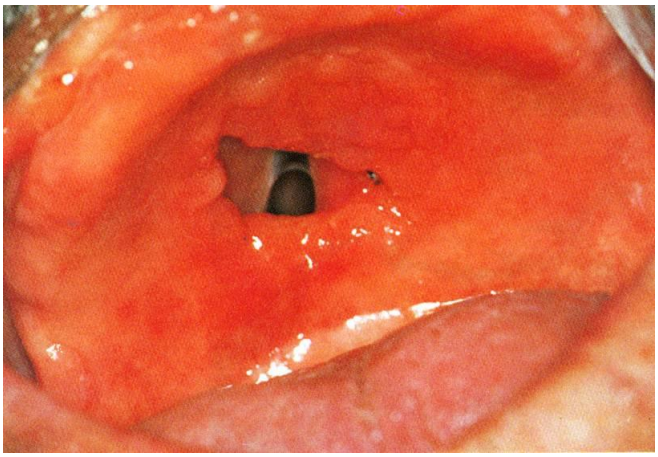


♥ **Tertiary or late stage syphilis:**

Develop many years after initial exposure. As Bacteria still latent in the Body, it will disseminate every where (walls of major Blood vessels, liver, kidney, lungs, and tongue).



Gummas (areas of necrosis associated with delayed type IV hypersensitivity reactions to syphilitic antigens) occur especially on hard palate leading to perforation into nasal cavity.



Histological features:

Gumma consists of central mass of coagulative necrosis surrounded by granulation tissue infiltrated by lymphocytes, plasma cells and macrophages with occasional giant cells.

Spirochaete are scanty or absent.

Atrophic glossitis is seen here and may be caused by *endarteritis obliterans*, smooth surface of tongue broken up by fissures from atrophy and fibrosis of tongue musculature

Endarteritis obliterans means the artery which is supplying a certain area becomes smaller artery then capillary when there is blockage of capillary or artery the area will die and necrosis will happened as no blood supply to this area and the blockage will happened by bacteria and its reaction.

Hyperkeratosis (syphilitic leukoplakia) follows which is premalignant and carcinoma of tongue develops. Now it is a rare factor in the aetiology of oral cancer.

Treated by penicillin.

♥ Congenital syphilis:

Infected mother can pass the Treponema Pallidum to her fetus and the fetus may die or there may be miscarriage or neonatal infection. If neonates survive the infection, we may see nasal bridge collapse.

Rare in affluent countries but in some community groups as drug abusers or those with lack of prenatal care including poorer countries of world.

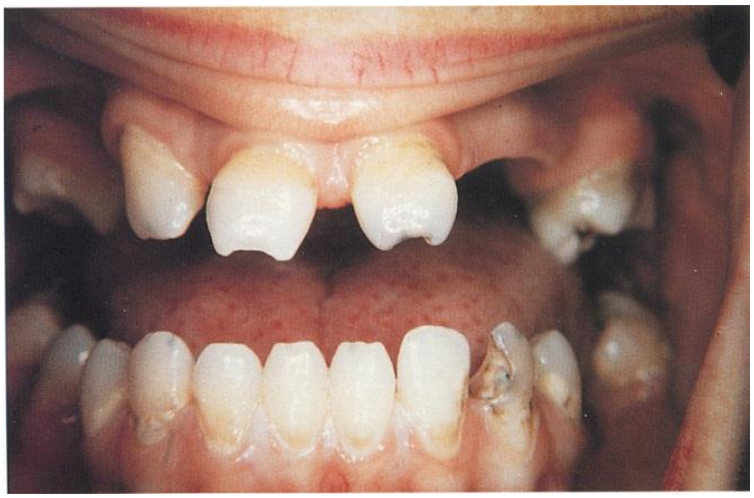
It is important cause of miscarriage, stillbirth and neonatal infection.

It is associated with infection of developing tooth germs of permanent incisors (Hutchinson's incisors) and first molars (moon's molars or mulberry molars which has globular masses of hard tissues on molars).

Note that Hutchinson triad is not only dental feature it is also defines and blindness.

Dental anomalies are tapered screw like incisors and peg shaped laterals.

Collapse of the bridge of nose due to infection and destruction of developing nasal bones produce the characteristic saddle deformity of the bridge and the dished appearance of face.



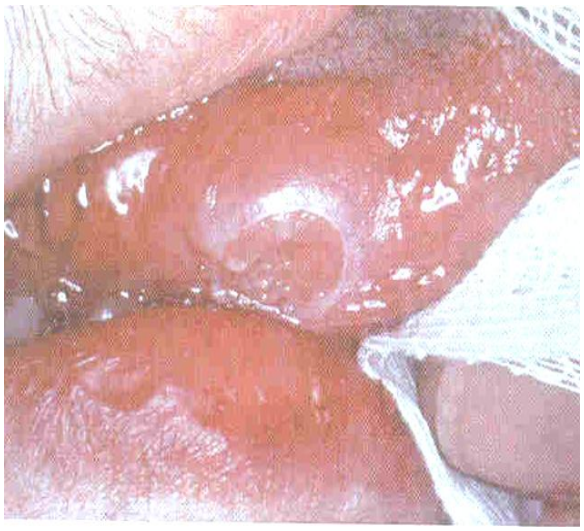
5- Tuberculosis (TB):

It is caused by *mycobacterium tuberculosis* which has a thick cell wall so can't be attacked by immune system easily, even macrophages may be can't attack it.

It can be latent in the lung, lymph nodes. It can be disseminate and reach kidneys or other organs causing severe diseases in the body.

The infection in oral cavity may be primary or secondary; it is primary if pt drink milk infected with the bacteria, secondary through coughing of infected sputum which make ulceration or infection in the oral cavity.

Most common features of secondary or oral TB is non-specific ulcer which is not really painful (some books say painless others say painful) but compared to size of ulcers the pain is minimal.



The ulcer margins are undermined (you can see coverage of the ulcer by tissue) covered by grayish slough necrotic material on surface and it is most commonly on the tongue because the coughed sputum may stay more on tongue.

Second feature is intraorally include Granulomatous reaction (we talked about it in Actinomycosis, syphilis, and TB and it is multinucleated giant cells, macrophages and give this appearance of hyperplastic rough and irregular).

The third feature is lymphadenitis (enlarged lymph nodes).

Diagnosis:

We need to see microspically Granulomatous inflammation, well defined granuloma and central necrosis.

Then we will ask the lab to give acid fast stain to see the acid fast bacilli appearing red, they are very small tiny rods of red bacteria.

Treatment needs 4-8 months by combination of antibiotics.

6- Leprosy:

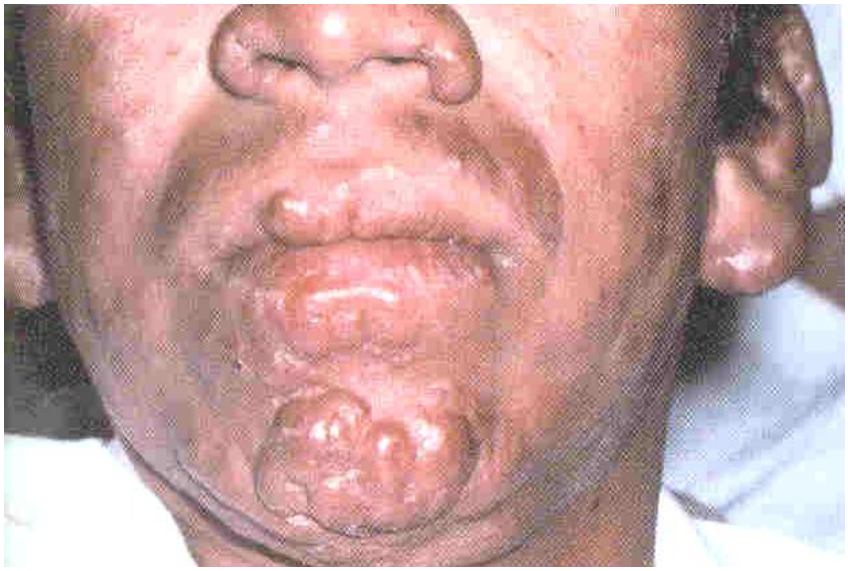
Infection caused by *mycobacterium "mycobacterium leprae*", occurs in endemic areas.

It is 2 forms; tuberculoid or lepromatous. The latter has poor prognosis than the first, there will be spread of the lesions.

oral involvement of lepromatous leprosy occurred when the nasal cavity is involved , and spread to the maxilla and the oral cavity which is more aggrieve than tuberculoid leprosy

Tuberculoid leprosy has well-defined granuloma, which indicate that the immune response is effective and strong in contrast to lepromatous leprosy.

Here there is rounded granuloma which means strong immune system, but if we find sheets of macrophages means not good immune system so spread of disease occurs and it will reach oral cavity.



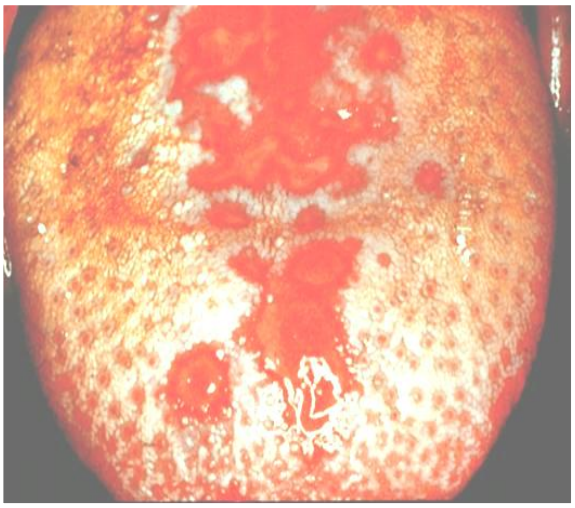
There will be facial deformity and nodules disfigurement in pt face, then ulceration, then fibrosis and pt will stay in this appearance.

Anterior gingival, maxilla, tongue, and palate are the most areas involved in oral cavity as it spread from nose.

7- Gonorrhea:

It is a venereal disease caused by *Neisseria gonorrhoea*.

It is non-specific oral features, pt has erythema (redness), vesicles, ulcerations and pain but not descriptive. Most of the pain appears on speaking and swallowing.



It is more in the posterior part on tonsils and soft palate mostly in sexually active adults.

Lesions reported from all areas of the mucosa.

تمت بحمد الله

Dr. Rima in this lecture realizes that guys talks more than girls so in our dof3a there are some differences than in the world.

"Tomorrow is a blank page, just waiting to be

filled with your dreams... All you have to do is be yourself and live the story of your own unique life.

Be proud. Be confident. And most of all be

happy.

Wish U all a happy new semester ☺

Kind regards,

M. Jaradat & H.AL-Katib